

Remarks

Claims 1-4, 6-8, 10 and 11 were pending in the subject application. By this Amendment, claims 1-3 have been amended, and claims 4, 6-8, 10 and 11 have been canceled. No new matter has been introduced by these amendments. Upon entry of these amendments, claims 1-3 will be before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Claim 2 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Applicants respectfully traverse and request reconsideration.

Indefiniteness is a question of law. *Praxair, Inc. v. ATMI, Inc.* 543 F.3d 1306, 1319 (Fed. Cir. 2008). The Court of Appeals for the Federal Circuit has stated:

The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, §112 demands no more. The degree of precision necessary for adequate claims is a function of the nature of the subject matter. *Miles Lab., Inc. v. Shandon, Inc.* 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993) (internal citations omitted) (emphasis added).

Applicants respectfully submit that the phrase “inserted at XbaI site” is definite under §112. XbaI site is well known in the art as 5' T ↓ C T A G A 3'. In addition, the complete genome of herpes simplex virus type 1 (HSV1, also called human herpes virus 1) has been mapped (*see* GenBank, X14112.1). Given the existing knowledge in the art, the specification further teaches at page 21, lines 23-25 that “HSV 1 genome segments loaded in cos6 and cos56 cosmids each have a XbaI single enzyme cutting site, respectively locating within nonessential genes UL2 and UL44, generally useful for inserting exogenous genes.” The location of the XbaI site is also illustrated in Figures 6-7. A skilled artisan, equipped with the existing knowledge regarding the entire genomic sequence of HSV-1, can readily determine where the XbaI site resides in UL2 and UL44, when further read in light of the specification. Therefore, the degree of precision required under §112 is satisfied. Accordingly, reconsideration and withdrawal of the rejection under §112, second paragraph, is respectfully requested.

Claims 1-3 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Applicants traverse, because one skilled in the art, given the existing knowledge in the art and further in view of teachings in the specification, would readily

recognize that Applicants were in possession of the full scope of the claim involving the insertion of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5 into a recombinant HSV1 genome.

The test for sufficiency of the written description is whether the application reasonably conveys to one skilled in the art that the inventor had possession of the claimed invention. *See, e.g., Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563; MPEP. 2163. The “written description” requirement must be applied in the context of the particular invention and the state of knowledge in the relevant art; it does not require that every invention must be described in the same way. *Capon v. Eshhar*, 418 F.3d 1349, 1358 (Fed. Cir. 2005). The descriptive text needed to meet these requirements varies with the nature and scope of the claim at issue, and with the scientific and technologic knowledge already in existence. In the *Capon* case, the Federal Circuit held that the Board erred in ruling that §112 imposes a *per se* rule requiring recitation of the nucleotide sequence of claimed DNA, when the sequence is already known in the field. *Id.* at 1357. The court states that “[i]t must be borne in mind that, while it is necessary that an applicant for a patent give to the public a complete and adequate disclosure in return for the patent grant, the certainty required of the disclosure is not greater than that which is reasonable, having due regard to the subject matter involved.” *Id.* at 1360.

None of the relevant legal precedents, e.g., *Regents v. Lilly*, *Fiers v. Revel*, *Amgen*, or *Enzo Biochem*, require a re-description of what was already known. Known information need not be determined afresh, and reanalysis of known elements is not required. *Capon v. Eshhar, supra*, at 1358.

Furthermore, “a patent claim is not necessarily invalid for lack of written description just because it is broader than the specific examples disclosed.” *Martek Biosciences Corp. v. Nutrinova, Inc.*, 2008-1459, -1476 at *9, (Fed. Cir. Sept. 3, 2009); *see also Bilstad v. Wakalopoulos*, 386 F.3d 1116, 23 (Fed. Cir. 2004). Indeed, courts have repeatedly “cautioned against limiting the claimed invention to preferred embodiments or specific examples in the specification.” *See, e.g., Martek Biosciences, supra*, at *9; *In re Rasmussen*, 650 F.2d 1212, 15 (CCPA, 1981); *Tex. Instruments, Inc. v. Int’l Trade Comm’n*, 805 F.2d 1558, 63 (Fed. Cir. 1986).

Claim 1 recites a recombinant herpes simplex virus type 1 (HSV1), comprising a heterologous nucleotide sequence selected from the group consisting of the sequences represented by SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5. Hence, the distinguishing characteristics of the genus are defined by the presence of the structure shown in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, or SEQ ID NO: 5.

Applicants further note that the nonessential gene region of the HSV1 genome recited in the present claims are readily distinguishable from the rejected claim elements in *Regents v. Lilly*, *Fiers v. Revel*, *Amgen*, or *Enzo Biochem*, which all involve unknown structures. By contrast, the entire genomic sequence of HSV1 is known. According to the Federal Circuit, the “written description” requirement must be applied in the context of the particular invention and the state of knowledge in the relevant art. *Capon v. Eshhar*, 418 F.3d 1349, 1358 (Fed. Cir. 2005).

To further illustrate, the complete genome of HSV1 has been mapped (*see* GenBank X14112.1; *see also*, for example, McGeoch, D. J. *et al.*, “Sequence determination and genetic content of the short unique region in the genome of herpes simplex virus type 1,” *J. Mol. Biol.* **181** (1), 1-13 (1985); McGeoch, D. J. *et al.*, “Complete DNA sequence of the short repeat region in the genome of herpes simplex virus type 1,” *Nucleic Acids Res.* **14** (4), 1727-1745 (1986); McGeoch, D. J. *et al.*, “The complete DNA sequence of the long unique region in the genome of herpes simplex virus type 1,” *J. Gen. Virol.* **69** (PT 7), 1531-1574 (1988); Perry, L. J. *et al.*, “The DNA sequences of the long repeat region and adjoining parts of the long unique region in the genome of herpes simplex virus type 1,” *J. Gen. Virol.* **69** (PT 11), 2831-2846 (1988)). The HSV-1 genome is a linear, double stranded DNA duplex, ~ 152,000 base pairs in length, and with a base composition of 67% G + C.

Furthermore, techniques for constructing HSV-1 mutants and modifying various cosmid in the whole HSV1 genome are known in the art (*see*, for example, Cunningham, C. and A. J. Davison, (1993), A cosmid-base system for constructing mutants of Herpes Simplex Virus Type 1, *Virology* **197**: 116-124, describing a cosmid-based system for constructing mutants of HSV1 using a total of five cosmids such as cos6, cos14, cos28, cos48, cos56; specification at page 17, lines 1-5). Consequently, HSV-1 has been frequently used as a “one vector cell/one helper virus for large-scale production of adeno-associated virus vector (specification at, for example, page 15, line 7 to page 16,

line 5 and page 11, lines 3-6). As the Patent Office is aware, none of these known information, such as the entire genomic composition of HSV1 and methods of constructing HSV1 variants, need be determined afresh since reanalysis of known elements is not required under §112. *Capon v. Eshhar* at 1358.

Given the existing knowledge in the art, the specification further provides numerous examples of actual reduction to practice regarding the introduction of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, or SEQ ID NO: 5 into a nonessential gene region (specification at, for example, page 4, line 7 to page 15, line 29; page 16, line 25 to page 23, line 8; Figures 6-8; Examples 1-1, 1-2, 2-1, 2-2, 3-1, 3-2, 4-1, 4-2, 5-1, and 5-2). The specification further specifies that the nonessential genes in the present invention refer to genes that are not essential for proliferation and passage of HSV1 in cells cultured *in vitro* (specification at page 15, lines 21-24).

Thus, it is within the level of skill and knowledge of those skilled in the art, who have been fully equipped with the entire genomic sequences of HSV1 as well as methods of constructing HSV1 mutants, to determine a nonessential gene region suitable for the insertion of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, or SEQ ID NO: 5. Further, those skilled in the art would recognize that Applicants were in possession of the full scope of the claim involving the insertion of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5 into a recombinant HSV1 genome. Accordingly, reconsideration and withdrawal of the rejections under §112, first paragraph, is respectfully requested.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the claims as currently pending are in condition for allowance, and such action is respectfully requested.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Respectfully submitted,



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